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EXAMINER
GOLDBERG, JEANINE ANNE

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/834,700	BRAUN, ANDREAS	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on th cov r sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-8, 11-20, 44-53, 69-71, 75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,11-20,44-53,69-71 and 75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed August 25, 2003. Currently, claims 1-8, 11-20, 44-53, 69-71, 75 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

3. Any objections and rejections not reiterated below are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-8, 11-20, 44-53, 69-71, 75 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well established utility.

The claims are drawn to an isolated nucleic acid molecule comprising a sequence of nucleotides that encodes a polypeptide as set forth in SEQ ID NO: 2 except at position 646 of SEQ ID NO: 2, Ile is substituted with Val, Leu or Phe. The claims are also drawn to primer, probes hybridizing to SEQ ID NO: 1 and at least 14 contiguous nucleotides from SEQ ID NO: 3 wherein at least 5 contiguous nucleotides are set forth in positions 2069-2077 of SEQ ID NO: 3.

The specification teaches that AKAP10 is located on Chromosome 17, contains 15 exons and 14 exons and has been found to be responsible for the sub-cellular

localization of the camp-dependent protein kinase (page 98, lines 28-32). The art teaches the AKAP10 cDNA (D-AKAP2) in Genbank Accession Number AF037439 and NM007202 (page 41). The specification teaches the detection of a single polymorphisms within the AKAP10 protein which causes a substitution of a Ile to a Val at position 646 of SEQ ID NO: 2 and a substitution of an A to a G at position 2073 of SEQ ID NO: 1. The specification asserts that the allelic variant has been found to vary in frequency in DNA samples from younger and older segments of a healthy population (page 43, lines 5-10). The specification similarly discusses AKAP10-1 allele which is located in the 3'UTR region. The specification performed similarly studies with regard to age related polymorphisms and determined that there was a difference between the populations.

The art teachesD-AKAP2 is a novel protein kinase A anchoring protein with a putative RGS domain. The cloning of a novel AKAP which interacts with both the type I and II regulatory subunits was reported as D-AKAP2 (Huang et al. PNAS, Vol. 94, pages 11184-111889, October 1997).

The specification nor the art has taught a substantial utility for a nucleic acid variant which comprises a single nucleotide polymorphism at position 2073 of SEQ ID NO: 3 which causes a substitution in the amino acid sequence at position 646. A substantial utility is defined as a utility that defines a "real world" us such that the utilities do not require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. The specification asserts that the nucleic acid is useful to determine increased or early susceptibility to morbidity. This assertion is not

substantial because further research to identify or reasonably confirm a "real world" context of use would be required.

The specification does not appear to support the conclusion that the AKAP10-5 G allele is associated with "increased susceptibility to morbidity, increased or early mortality, or morbidity and increased or early mortality as compared to the susceptibility of a subject who does not comprise the allelic variant" (page 15). The study performed in the specification was performed using healthy samples through the blood bank of California. The donors were of Caucasian origin. The specification asserts that a healthy subject is defined as human donor who passes blood bank criteria to donate blood. An analysis of data is presented in Table 4 stratified by males and females by age groups (page 103-104). The data does not appear to suggest that there is an increase susceptibility to morbidity because in males who are heterozygous for GA at position 2073 of SEQ ID NO: 1, more "older" individuals than "younger" individuals are found. Therefore, the assertion that the presence of a G increases susceptibility does not appear to be consistent with the date. The data provides that 45.9% of younger individuals have GA whereas 52.5% of older individuals have GA. Therefore, the date with respect to men does not appear to support the conclusion. Additionally, for the combined sexes, the data also suggests that GA individuals are very slightly more likely to be found in older populations. 47.7% vs 49.4% were found in younger and older populations respectively to have the GA herterozygosity. Therefore, the conclusion that the variant G allele is associated with increased susceptibility to morbidity does not appear to be supported by the data. When considering the pure analysis of G and A

alleles, the minimal difference of 4.1% between young and old populations would require the researcher to further analyze the information to determine whether the polymorphism was meaningful. Give the information in Table 3, using a statistical calculation website to determine the 2x2 contingency table, the p-value provided by the website was p=.13 which is not statistically significant.

gttp://faculty.vassar.edu/lowry/odds2x2.html

It is additionally noted that the specification fails to study an ethnically diverse population. The specification states that only Caucasian individuals were analyzed and a very minimal difference was found. The specification teaches a mere difference of 60 and 64% between the two populations. The skilled artisan would be required to perform additional experimentation to determine whether this particular population is representative of the entire world population or whether this was merely applicable to Caucasian individuals.

The specification does not analyze individuals in a progressive study of their lifetime but rather takes a current snapshot of the percent frequencies of the particular SNP. Therefore, it is unpredictable whether the original populations of younger and older initially contained the same frequencies of alleles. If the polymorphism was regionally isolated, the event of mobility of the younger population would explain the variation of the polymorphisms within the populations. For example, if elderly Californians remain relatively settled within the region, and younger individuals migrate to the region, the frequencies of the polymorphism may vary. Without further analysis of the original older population of allele frequencies it is unclear how these frequencies

have changed. In the event that the nucleotide is environmentally sensitive and has either been selected against. Furthermore, if the polymorphism is located within a region of the gene which is a hotspot and naturally mutates in an individuals life, frequencies of the variation would change over time and would not be a reliable predictor of mortality. Additionally, whether the change is in response to certain environmental causes, the presence of a variant G allele is not predictable. The specification does not analyze individuals who are deceased for the presence of various alleles. Had the specification demonstrated that deceased individuals contained more G alleles in conjunction with the instant study illustrating that young individuals had A, a more conclusive analysis may be drawn. The specification is silent with respect to any analysis of T or C.

The is no correlation supported for T and C nucleotides at position 2073 of SEQ ID NO: 1. It is unpredictable whether these mutations would also be associated with any type of disease.

The art is silent with respect to additional mutations within the subcellular localization of camp-dependant protein kinase and therefore, not well characterized as to how affect mortality or morbitiy.

Additionally, there is no indication of what meant by increased mortality. The specification has defined "mortaility" as the statistical likelihood that an organism will not survive a full predicted lifespan. The specification has not provided any indication that the individuals analyzed have not survived a full predicted lifespan. Moreover, it is

unclear what the relative meaning of increased mortality encompasses since all individuals are predisposed to die.

With respect to Claim 44, directed to a cell comprising a nucleic acid that encodes a human AKAP10 variant protein or portion that exhibits a biological activity of the full length variant protein wherein the AKAP10 variant protein or portion thereof comprises valine at position corresponding to the position of amino acid residue 646 of SEQ ID NO: 2. The specification has provided a single human AKAP10 variant protein, namely a substitution at amino acid position 646 of SEQ ID NO: 2. The specification does not particular provide any additional variant proteins that exhibit a biological activity of the variant protein. The specification fails to provide any biological activity information for the variant protein to constitute a function, therefore, determining whether the portion exhibits biological activity has not been described. Therefore, determining the function of the variant protein would require and constitute carry out further research to confirm a real world context of use.

As noted by Brenner v. Manson, 383 U.S. 519, 535-536 (1996), "Congress intended that no patents be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing...a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion". Therefore, in order to reasonably confirm a "real world" context of use for this nucleic acid, the skilled artisan would be required to carry out further research.

Response to Arguments

The response traverses the rejection. The response asserts the claimed inventions have clear, specific and unquestionable utility as they specification teaches screening assays for analyzing compounds (page 10-11 of response filed August 25, 2003). The response further asserts that the alteration in signal transduction biological activity is reasonably correlated to specific disease, such as diabetes, cardiomyopathies, and the like. The response asserts that the nucleic acids are useful in nucleic acid detection methods for detecting the particular allelic variant (page 12 of response filed August 25, 2003).

It is noted that applicant's have not addressed the association of the polymorphic region with morbidity as extensively discussed in the rejection above.

The seminal decision interpreting the utility requirement of § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [it] is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as
> man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.[1]

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of

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[1] The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one

skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler

was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

The asserted utility of the claimed polynucleotides—as a component of a screening assay for potential therapeutics—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

Assume, for example, that an isolated nucleic acid molecules comprising a sequence of nucleotides that encodes a polypeptides as set forth in SEQ ID NO:2, except the Ile residue at position 646 of SEQ ID NO; 2 is replaces with Val, Leu, or Phe is placed in a cell and the researcher observed that signal transduction was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in signal transduction would depend on other factors, but again the specification provides no hint what other factors might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using AKAP10-5 in screening assays for potential therapeutics or screening assays that modulate altered signal transduction, screening assays to identify compounds that modulate AKAP10 biological activities related to AKAP10 binding to PKA, AKAP10 localization to the mitochondria, binding to other signaling enzymes and phosphorylation by PKA.

In effect, applicant's position is that the claimed polynucleotides are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. Applicant asserts that

such a disclosure provides a "clear, specific and unquestionable utility." Rather, the instant case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, the applicants claim a product asserted to be useful in a method of screening, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the product claims here lack utility, based on their use in screening arrays, because the specification does not disclose how to use the AKAP10-5 data generated by a screening assays for potential therapeutics. Moreover, the instant specification fails to demonstrate that methods of detecting a particular allelic variant is useful for more than studying the nucleic acid itself.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8, 11-20, 44-53, 69-71, 75 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a

substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 6-8, 11-18, 44, 47-50, 69-71, 75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 6-8, 15-18 are drawn broadly to encompass any isolated nucleic acid which comprises at least 16, 30, or 50 contiguous nucleotides of SEQ ID NO: wherein the contiguous nucleotide include 5 contiguous nucleotides from position 2069-2077 of SEQ ID NO: 3. The claim as written minimally comprises 16, 30 or 50 contiguous nucleotides of SEQ ID NO: 3 embedded within a larger sequence. As noted by the art cited in rejections below, the instant specification has not described a representative number of members within this very large genus. There is actual reduction to practice of a single disclosed species, namely SEQ ID NO: 3. The genus of nucleic acids comprising at least 16, 30 or 50 contiguous nucleotides from SEQ ID NO: 3 encompasses splice variants of AKAP10-5, polymorphic sequences of AKAP10-5, a full length gene which contains the fragment and homologous sequences which have not

been described. There is substantial variability among the species of DNA s encompassed within the scope of the claims because the claim is only drawn to a fragment of SEQ ID NO: 3 which may be embedded in alternative sequences.

Claims 11-14, 47-50, 69-71 is drawn to an oligonucleotides which comprises a sequence of nucleotides that specifically hybridizes adjacent to or at a polymorphic region spanning a position corresponding to position 2073 of SEQ ID NO: 1 or 3. The specification defines "adjacent" as a position 5' to the sit of a SNP such that there could be unpaired nucleotides between the position and the site of the SNP (page 40, lines 14-16). Claim 69 is drawn to a solid support comprising a nucleic acid comprising a polymorphic region of an AKAP10 gene, wherein the polymorphic region comprises a nucleotide at a position corresponding to position 2073 of SEQ ID NO: 1 that is other than an A. As defined by the specification, a nucleic acid which "corresponds" to the nucleic acid may be of different length, such that the sequences are aligned and then the position that lines up with 2073 is identified (page 38-39). This does not require any particular sequence flanking the nucleotide "other than A." The claim encompasses any size nucleotide sequence, which hybridizes under any conditions upstream of position 2073 of SEQ ID NO: 1 or 3 or any sequence which "corresponds" to position 2073. Thus, the "corresponding" sequence does not require any particular similarity or identity with SEQ ID NO: 1 or 3. Moreover, Claim 13 requires that the primer hybridize immediately adjacent to a position corresponding to a position corresponding to position 2073. As discussed above, "corresponding" does not require that the sequence resemble SEQ ID NO: 1 or 3. Moreover, depending on the interpretation of the

recitation "a sequence of nucleotides that specifically hybridizes adjacent to or at a polymorphic region spanning a position corresponding to position 2073 of SEQ ID NO: 1 or 3 of an AKAP10 allele..." the claim may lack description. Because it is unclear whether the claim is directed to a sequence of nucleotides that specifically hybridizes adjacent to an AKAP10 allele, the specification has only described a single allele within the scope of the claims. The description of this single variant is not representative of all AKAP10 alleles. The nature of variants is such that the indication of a single variant allele is not representative of unknown alleles. The variant structures, in the present state of the art, of one variant does not provide guidance to the structure of others.

Claim 44 is directed to a cell comprising a nucleic acid that encodes a human AKAP10 variant protein or portion that exhibits a biological activity of the full length variant protein wherein the AKAP10 variant protein or portion thereof comprises valine at position corresponding to the position of amino acid residue 646 of SEQ ID NO: 2. The specification has described a single human AKAP10 variant protein, namely a substitution at amino acid position 646 of SEQ ID NO: 2. The specification does not particular provide any additional variant proteins that exhibit a biological activity of the variant protein. The specification fails to provide any biological activity information for the variant protein to constitute a function, therefore, determining whether the portion exhibits biological activity has not been described. Furthermore, the claim encompasses additional mutations, splice variants and transitions which have not been described in the instant specification. The nature of variants is such that the indication of a single variant allele is not representative of unknown alleles. The variant

structures, in the present state of the art, of one variant does not provide guidance to the structure of others.

Claim 75 is drawn broadly to a primer consisting essentially of a nucleotide selected from SEQ ID NO: 8, 15, 19 and 20. The nucleic acid reads on any oligonucleotide which comprises SEQ ID NO: 8, 15, 19 and 20 which vary in length from 17-20 nucleotides. As discussed above, the partial structure embedded within a larger sequence is not representative of the entire genus, as exemplified by the art rejections below.

Therefore, one of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim.

Response to Arguments

The response traverses the rejection. The response asserts that the claims do not require splice variants of AKAP10-5, polymorphic sequences, full length genes or homoglous sequence. The response admits that the nucleic acids may be present within the claimed subject matter, but are not required. This argument has been reviewed but is not convincing because the claims broadly encompass each of these variants which applicant was not in possession of at the time of filing. One of skill in the art would have concluded that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the

variants of the genus and is insufficient to support the claim. The written description requirement is directed to the possession of the applicant of the claimed subject matter.

Claim 11 has been amended to require 16 nucleotides and high stringency conditions. The response further argues that the skilled artisan would understand that a corresponding position to be at least 95% identical with the reference sequence. As seen in Written Description Example 9, claims drawn to cDNA which hybridize under highly stringent conditions, and provide a function may be found to be described. However, the instant claims are drawn to partial sequences, and lack any particular function. The specification specifically indicates that the concept of corresponding does not mean identity with the flanking sequences. Therefore, the claims encompass large numbers of nucleic acids which have neither been reduced to practice or described.

The rejection as it applies to Claim 44 has been traversed. The response asserts that that the protein must contain a Val at residue 646 of SEQ ID NO: 2. This argument has been thoroughly reviewed, but is not found persuasive because the claim does not require SEQ ID NO: 2, but merely requires a AKAP10 variant protein with a valine. The protein may contain additional variants, mutations, truncations which have not been described. One of skill in the art would have concluded that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim.

Applicant traverses the rejection as it applies to Claim 75. The response asserts that consisting essentially of is not the same as comprising. The MPEP 2111.03 states,

> "for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) ("Although consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of' language.").

The specification teaches that primers may hybridize to a nucleic acid and have the ability to amplify. There is no length limitation for the claimed sequences. Any nucleic acid which was not blocked on the 3' end would be functional as a primer.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claim 75 is rejected under 35 U.S.C. 102(b) as being anticipated by Birren et al. (Genbank Accession Number AC005730, October 1998).

The claim is directed to a primer consisting essentially of nucleotide sequences selected from the group consisting of SEQ ID NO: 8, 15, 19 and 20. Consisting essentially of has been interpreted broadly as "comprising." It is noted that the recitation "primer" has been given no weight for the intended use. The specification specifically teaches that primers can be 10, 20, 30, 50, 100 or more nucleotides in length, i.e. not specifically limiting the length of a primer.

Birren et al. (herein referred to as Birren) teaches a nucleic acid clone from chromosome 17 which comprises all 18 nucleotides of SEQ ID NO: 20. Nucleotides 1-18 of SEQ ID NO: 20 are identical to positions 129,582-129,599 of the chromosome 17 nucleic acid. Therefore, Birren teaches a nucleic acid comprising SEQ ID NO: 20 as required by the instant claim.

Response to Arguments

The response traverses the rejection. The response asserts that the word primer limits the claims because the basic and novel characteristic of the claims primers is the capability of hybridizing adjacent to the polymorphic region of interest for subsequent nucleotide extension from the 3' end of the primer. The MPEP 2111.03 states,

> "for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893,

> 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) ("Although consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of' language.").

The specification states that primers refer to nucleic acids which are capable of specifically hybridizing to a nucleic acid which is adjacent to a polymorphic region of interest or to a polymorphic region and are extended (page 61, lines 2-13). This argument has been reviewed but is not convincing because the nucleic acid of SEQ ID NO: 20 is 100% identical to the cited nucleic acid, therefore would be capable of specifically hybridizing to the nucleic acid, as defined by the specification. The claimed invention is drawn to SEQ ID NO: 20, therefore, the definition of primer is not clear as it pertains to binding to a polymorphic region or a polymorphic region. There is no indication of record that the cited nucleic acid could not be extended. In the event that applicant thinks that primer carries a particular length limitation, applicant may limit their claims to a particular length which is supported by the specification.

Thus for the reasons above and those already of record, the rejection is maintained.

8. Claim 75 is rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al. (Genbank Accession Number AA331406, April 1997).

The claim is directed to a primer consisting essentially of nucleotide sequences selected from the group consisting of SEQ ID NO: 8, 15, 19 and 20. Consisting essentially of has been interpreted broadly as "comprising." It is noted that the recitation "primer" has been given no weight for the intended use. The specification specifically teaches that primers can be 10, 20, 30, 50, 100 or more nucleotides in length, i.e. not specifically limiting the length of a primer.

Adams teaches a nucleic acid from an embryo, 8 week I Homo sapiens cDNA. The nucleic acid comprises all 19 nucleotides of SEQ ID NO: 19. Nucleotides 1-19 of SEQ ID NO: 19 are identical to positions 45-27 of the human nucleic acid. Therefore, Adams teaches a nucleic acid comprising SEQ ID NO: 19 as required by the instant claim.

Response to Arguments

The response traverses the rejection. The response asserts that the word primer limits the claims because the basic and novel characteristic of the claims primers is the capability of hybridizing adjacent to the polymorphic region of interest for subsequent nucleotide extension from the 3' end of the primer. The MPEP 2111.03 states,

> "for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention.

In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) ("Although consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of' language.").

The specification states that primers refer to nucleic acids which are capable of specifically hybridizing to a nucleic acid which is adjacent to a polymorphic region of interest or to a polymorphic region and are extended (page 61, lines 2-13). This argument has been reviewed but is not convincing because the nucleic acid of SEQ ID NO: 19 is 100% identical to the cited nucleic acid, therefore would be capable of specifically hybridizing to the nucleic acid, as defined by the specification. The claimed invention is drawn to SEQ ID NO: 19, therefore, the definition of primer is not clear as it pertains to binding to a polymorphic region or a polymorphic region. There is no indication of record that the cited nucleic acid could not be extended. In the event that applicant thinks that primer carries a particular length limitation, applicant may limit their claims to a particular length which is supported by the specification.

Thus for the reasons above and those already of record, the rejection is maintained.

9. Claim 75 is rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al. (Genbank Accession Number AA349877, April 1997).

The claim is directed to a primer consisting essentially of nucleotide sequences selected from the group consisting of SEQ ID NO: 8, 15, 19 and 20. Consisting

essentially of has been interpreted broadly as "comprising." It is noted that the recitation "primer" has been given no weight for the intended use. The specification specifically teaches that primers can be 10, 20, 30, 50, 100 or more nucleotides in length, i.e. not specifically limiting the length of a primer.

Adams teaches a nucleic acid from an infant brain Homo sapiens cDNA. The nucleic acid comprises all 18 nucleotides of SEQ ID NO: 15. Nucleotides 1-18 of SEQ ID NO: 19 are identical to positions 198-181 of the human nucleic acid. Therefore, Adams teaches a nucleic acid comprising SEQ ID NO: 15 as required by the instant claim.

Response to Arguments

The response traverses the rejection. The response asserts that the word primer limits the claims because the basic and novel characteristic of the claims primers is the capability of hybridizing adjacent to the polymorphic region of interest for subsequent nucleotide extension from the 3' end of the primer. The MPEP 2111.03 states,

> "for the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of "consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also Ex parte Hoffman, 12 USPQ2d 1061, 1063-64 (Bd. Pat. App. & Inter. 1989) ("Although consisting essentially of' is typically used and defined in the context of compositions of matter, we find nothing intrinsically wrong with the use of such

> language as a modifier of method steps. . . [rendering] the claim open only for the inclusion of steps which do not materially affect the basic and novel characteristics of the claimed method. To determine the steps included versus excluded the claim must be read in light of the specification. . . . [I]t is an applicant's burden to establish that a step practiced in a prior art method is excluded from his claims by consisting essentially of' language.").

The specification states that primers refer to nucleic acids which are capable of specifically hybridizing to a nucleic acid which is adjacent to a polymorphic region of interest or to a polymorphic region and are extended (page 61, lines 2-13). This argument has been reviewed but is not convincing because the nucleic acid of SEQ ID NO: 15 is 100% identical to the cited nucleic acid, therefore would be capable of specifically hybridizing to the nucleic acid, as defined by the specification. The claimed invention is drawn to SEQ ID NO: 15, therefore, the definition of primer is not clear as it pertains to binding to a polymorphic region or a polymorphic region. There is no indication of record that the cited nucleic acid could not be extended. In the event that applicant thinks that primer carries a particular length limitation, applicant may limit their claims to a particular length which is supported by the specification.

Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

10. No claims allowable.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg
Jeanine Goldberg
November 13, 2003

JEHANNE SOUAYA
~~PATENT~~ EXAMINER
Primary
Jehanne Souaya
11/13/03